ral structure initially discovered (SN: 8/17/85, p. 102). For example, in the Sept. 30 PHYSICAL REVIEW LETTERS, Leonid Bendersky of the Johns Hopkins University in Baltimore reports the formation of a decagonal phase, which has neatly stacked layers, each showing a nonperiodic, 10-fold symmetry.

Despite the recent flood of research papers devoted to quasicrystals, the theoretical interpretation of the results as a genuinely new crystalline structure remains controversial. In the Oct. 10 NATURE, Linus C. Pauling of the Linus Pauling Institute of Science and Medicine in Palo Alto, Calif., argues that the "icosahedral" structures are really "multiple twins of a cubic crystal."

Pauling proposes that aluminum-manganese alloys, when suddenly cooled, solidify into a cubic form in which each unit contains about 1,120 atoms. About 20 crystals, made up of these cubic units and roughly tetrahedral in shape, could grow out from a central seed to produce an approximate icosahedral shape. Pauling's structure seems to account for the way X-rays diffract from powdered samples of the new materials.

"Crystallographers can now cease to worry that the validity of one of the accepted bases of their science has been questioned," Pauling concludes.

"I'm certainly not convinced that he [Pauling] has the correct explanation for all of the experiments," says Harvard physicist David R. Nelson. "I'm skeptical that his model will account properly for a single-crystal diffraction pattern."

Nelson's comments are typical of the reaction among quasicrystal researchers. Although Pauling's structure seems to work for a powder, consisting of a host of tiny crystals sitting in random positions, it doesn't work, they say, for the distinctive pattern of spots seen in a single-crystal electron diffraction experiment.

"This material really is a quasicrystal," says Steinhardt, "but one that has a lot of defects in it. We'd really like to have a more perfect sample." This would allow researchers to check more closely proposed theories about the structure of the new materials. —*I. Peterson*

Is ozone giving acid rain a bad name?

Ozone, the most plant-damaging gaseous pollutant, decreases photosynthesis and promotes premature leaf aging, a new study reports. The study also suggests that ambient levels of this pollutant, in all but high-elevation areas, may account for much of the U.S. forest damage previously attributed to acid rain.

The study, conducted by researchers at the Boyce Thompson Institute at Cornell University in Ithaca, N.Y., focused on measuring how rates of photosynthesis changed among crop plants (soybeans, wheat and clover) and trees (white pine, hybrid poplar, sugar maple and red oak) exposed to different levels of ozone. Pollutant levels, from 0.02 to 0.14 parts per million (ppm) in air, were "realistic" — characteristic of mean, daylight concentrations actually observed in regions ranging from pristine areas to agricultural regions of the central United States to heavily polluted southern California. Plants were fumigated, either in the field or in controlled laboratory chambers.

Writing in the Nov. 1 SCIENCE, Peter Reich and Robert Amundson report that the ozone vulnerability of a plant species seems to be related to the rate at which gases can enter its leaves — a factor determined by their pores, called stoma. Species with high rates of growth and photosynthesis, such as crop plants, tend to have larger stomal openings — and therefore greater ozone uptake — explains Reich, who is now at the University of Wisconsin in Madison.

In the study, ozone-related declines in photosynthesis occurred among all species and at all concentrations. The rate of damage, however, was unique to each: Clover, wheat and soybeans were most vulnerable; red oak and white pine were least so. For instance, an internal ozone dose of 10 ppm-hr (ppm concentration multiplied by exposure time) brought a 50 percent reduction in wheat photosynthesis and a near 50 percent decline in yield. By contrast, a threefold higher dose to white pine brought only a 10 percent drop in photosynthesis and growth or yield. Finally, although there were no visible signs of acute ozone poisoning (mottled discoloration) in exposed leaves, the time it took a leaf to mature, discolor and drop decreased as ozone exposure increased — suggesting, Reich says, that the pollutant accelerates leaf aging.

When the tests were repeated using water with a pH comparable to that of acid rain, there was no additional decrease in photosynthesis, acceleration in leaf aging or change in plant growth and yield.

These findings came as no surprise to Allen Heagle, a plant pathologist in Raleigh, N.C., who is involved with the four-state, four-year-old National Crop Loss Assessment Network, the nation's largest program studying ozone's effects on plants. "Ozone is clearly the bad guy here," Heagle says. What's more, he says, "In everything we've done with crops here, we find that at ambient levels ozone is much more of a factor [than acid rain]." The big unknown, he says, is how badly ozone is hurting trees, since "there are no studies that have looked at the long-term effects of ozone on trees."

Curbing ozone will be no easy trick, Reich and Heagle point out, since the largest source of the pollutant's chemical precursors is auto exhaust. —*J. Raloff*

Estrogen use raises questions

Estrogen, it seems, may be one of those things some women can't live with and can't live without. Replacing the class of hormones lost as a result of menopause or surgical removal of the ovaries can alleviate the discomforts of menopause and prevent the bone-breaking disease of osteoporosis. But postmenopausal estrogen use is also associated with endometrial cancer, and depending on which of two current studies you believe, it can reduce or increase the risk of heart disease.

While some 2 million to 3 million postmenopausal women in the United States take estrogens daily, scientists are struggling to determine if the practice is ultimately helpful or harmful. In addition to the two studies alternatively associating the hormones with a higher and a lower risk of heart disease, a recent report shows an increased risk of endometrial cancer not just in women currently using estrogens but in past users as well.

The incidence of heart disease in both pre- and postmenopausal women is much lower than it is in men. According to the National Center for Health Statistics in Hyattsville, Md., the heart disease death rate in 1982 among 35- to 44-year-old men was 44 per 100,000, and only 10 per 100,000 among women. In the 65- to 74-year-old range, it was 1,268 per 100,000 men and 568 per 100,000 women. The influence of estrogens has long been suspected as the operative agent. In fact, men who were considered likely candidates for heart attacks were at one time given estrogens as a preventive, until it was shown that the practice put such men at higher risk.

Two studies in the Oct. 24 NEW ENGLAND JOURNAL OF MEDICINE go head-to-head on the heart disease question. One is an analysis of data from the Framingham Heart Study, a collection of medical information regarding the inhabitants of a Massachusetts town. Peter W.F. Wilson and William P. Castelli of the Framingham study and Robert J. Garrison of the National Heart, Lung, and Blood Institute in Bethesda, Md., followed up on 1,234 postmenopausal women who had been questioned between 1970 and 1972 about their estrogen use.

Of these women, 302 had used estrogens after they reached menopause; 932 had not. All were over 50 at the beginning of the Framingham study.

Eight years later, the estrogen users scored better than nonusers on an analysis of various risk factors known to be associated with cardiovascular disease — including blood pressure, weight and the blood level of total cholesterol and its individual components. Despite the apparent advantage, the researchers report that "significant detrimental effects were seen for total cardiovascular disease, coronary

heart disease and stroke in particular."

They had statistically removed the effects of "confounding variables." For example, if it happens that fewer women who are on estrogens smoke, it would make estrogens look good — but the favorable outcomes might be attributable to abstention from smoking, a known cardiovascular risk factor, rather than to estrogens. So the researchers factored out the effects of age, blood pressure, weight, cholesterol levels, smoking and alcohol use, and calculated the relative risk.

The incidence of coronary heart disease, including heart attacks and reported chest pain, among the women who used estrogens was 1.9 times the rate in nonusers. The users' risk of cerebrovascular disease, including stroke, was 2.2 times the level in nonusers. Despite these higher risks, the overall risk of death from whatever cause was essentially the same in the two groups.

"No benefits from estrogen use were observed in the study group," the researchers conclude.

In contrast, a study in the same issue of the NEW ENGLAND JOURNAL suggests that estrogens *protect* against heart disease. Six researchers from Harvard University looked at data collected in a large, long-term epidemiological project, in which periodic questionnaires were mailed to 121,964 female nurses who were between 30 and 55 in 1976.

The scientists examined the rate of heart disease among 32,317 initially healthy postmenopausal women, about half of whom had at some time used estrogens. By 1980, 90 women had had nonfatal heart attacks, and another 65 had died of heart attacks.

The Harvard researchers found that, overall, the death rate from heart disease among the nurses who had used estrogens was half that of the women who had never used them; the duration of estrogen treatment was not a factor.

The protective effect held when the researchers factored out known risk factors — parental history of heart attacks, past oral contraceptive use, smoking history, high blood pressure, high cholesterol, diabetes and ovarian removal.

"The results of this prospective study and other investigations are consistent with the hypothesis that postmenopausal hormone use markedly reduces the risk of coronary heart disease among postmenopausal women," they report.

What does it mean when two epidemiological studies show opposite results? In an accompanying editorial in the journal, Harvard's John C. Bailar III says both studies are methodologically sound. There are, he observes, some obvious differences in the studies — the method of data collection, length of follow-up, nature of hormone treatment, statistical methods and other factors — but not enough to account for the opposite conclusions.

Bailar suggests that there are other factors not adequately reflected in the data and statistical models — age, for example, or higher rates of smoking in Framingham women, or differential use of estrogen between the two groups.

Neither study is perfect. Several epidemiologists have already criticized the Framingham study for looking only at whether the women had been taking estrogens eight years earlier rather than determining if they had taken estrogens in the intervening years. Framingham researcher Wilson says that, based on other data, he expects that use or nonuse did not change appreciably after the study began.

In the Framingham multifactor analysis, which attempted to single out the independent role of estrogens, the effect of cholesterol levels was excluded. Since estrogens are believed to work by lowering cholesterol levels, factoring cholesterol out might be expected also to factor out the benefits of the hormone, says Meir J. Stampfer of Harvard, one of the authors of the nurse study. To this Wilson responds, "It's a methodology issue. We would have been chided no matter which way we went."

The idea, Wilson says, was to determine estrogens' role in heart disease over and above their effect on cholesterol. He notes that an earlier study by another group showed that the healthier levels of a cholesterol-related component couldn't completely explain estrogens' salutary effects, so there is some precedent for excluding it. Still, the Framingham researchers are planning on using a different model to look at the effect of estrogens without excluding cholesterol levels, Wilson says.

Another criticism made by Stampfer and others is that angina (chest pain) was counted as heart disease. This, he says, could have inflated the total incidence of cardiovascular illness, since angina is not necessarily a forerunner of heart disease.

The nurse study has its own problems. It relies on women who are presumably more health-aware than the general population — hence they may be less likely to have heart attacks.

In addition, Framingham's Wilson points out, the 30- to 55-year-old nurses included in the study had all reached menopause, meaning many of them had ceased menstruating at an unusually early age, and many had had ovariectomies and hysterectomies.

Wilson believes that such differences between the studies may help explain the discrepancy in conclusions. "We have an old group," he says. "Their study ends at age 55; that's where our study begins." And many more of the nurses had a history of oral contraceptive use, a possible confounding variable, than the Framingham women.

"I don't know if all the differences can completely explain [the findings]," says Stampfer. The question, says Wilson, is far from resolved, and resolving it isn't going to be easy. He and several other epidemiologists note that the ideal study would monitor illness and death in postmenopausal women arbitrarily assigned to receive either estrogens or a placebo. Such a study would be difficult, he says, because most of the researchers in the field have a definite opinion as to estrogens' values and dangers, and would balk at assigning women to a randomized study. In addition, researchers would need to consider an enormous amount of additional data — the age at which a woman begins taking estrogens, the type of estrogens used and duration of use, for example.

In the meantime, what's a woman to do?

"A judgment about whether hormones should be routinely prescribed for prophylaxis [of menopausal symptoms and osteoporosis] must be tempered by a consideration of other associated risks and benefits," the scientists from Harvard say. "It's something a woman has to weigh with her physician," says Stampfer.

The Framingham group concludes that "the potential drawbacks to postmenopausal estrogen therapy should be considered carefully before recommending its widespread use."

"The decision is an important one to be made between the patient and her physician," says Neil B. Rosenshein of Johns Hopkins in Baltimore, who was involved in an endometrial cancer study that appeared in the Oct. 17 NEW ENGLAND JOURNAL OF MEDICINE. He and his colleagues found that postmenopausal exposure to estrogens increases the risk of endometrial cancer for as long as 10 years after usage stops; they recommend that women on "replacement" estrogen therapy be considered for long-term gynecological surveillance. Women who've had their uteruses removed and who want to take estrogens to relieve menopausal symptoms or prevent osteoporosis have an easier choice, he notes, since they can't get endometrial cancer.

Elizabeth Barrett-Connor of the University of California at San Diego and Trudy L. Bush of Columbia University in New York surveyed the literature on cardiovascular disease and estrogen use in EPIDEMIOLOGIC REVIEWS (Vol. 7, 1985). The majority agree with the nurse study, Barrett-Connor says.

Barrett-Connor has also conducted a study on estrogen and mortality. After factoring out smoking and age, she found a 50 percent lower death rate among estrogen users than among nonusers, suggesting less heart disease.

In his editorial, Bailar asks the key question: "What are we to believe at this point?" His answer: "I simply cannot tell from present evidence whether these hormones add to the risk of various cardiovascular diseases, diminish the risk or leave it unchanged, and must resort to the investigator's great cop-out: More research is needed." —*J. Silberner*